Notice of Allowability	Application No. 10/668,696	Applicant(s) KELLER ET AL.	
	Examiner William W. Moore	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendments filed 18 July and 27 September, and the interview of 27 September, 2005*.

2. ☒ The allowed claim(s) is/are *7,9,11-14,16-20,23-27 and 33-36*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Response to Amendment

Applicant's Amendments to the specification filed 18 July and 27 September 2005, and a revised Sequence Listing in both printed and computer-readable forms submitted 18 July September 2005 have been entered and overcome the objections of record to the specification for an absence of sequence identifiers at page 64 of the specification and for presence of activatable hyperlinks should the patent be viewed on the Internet. It is agreed that the amendments to the specification add no new matter to the disclosure. Applicant's cancellations of claims 1-6, 21-22 and 28-32, the amendments to claims 7, 8, 10, 12-17, 23, 24, and 27, and the new claims 33-37 in the amendment filed 18 July September 2005 were also entered. The following Examiner's Amendment further amends several examined claims and as well as further claims rejoined pursuant to provisions of MPEP § 821.04 where a desired scope commensurate with the product described by the amended claim 7 could be agreed upon, permitting the allowance of claims 7, 9, 11-14, 16-20, 23-27, and 33-36 herewith.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Cancel claims 8, 10, 15 and 37.

Amend claims 7, 9, 11-14, 16, 18, 20, 23, 25, 27, 33, 34 and 36 thus:

7. (Amended) An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

(a) ~~a~~ the nucleotide sequence set forth in SEQ ID NO:2 ~~encoding a methyltransferase~~;

(b) a nucleotide sequence encoding ~~an~~ the amino acid sequence set forth in SEQ ID NO:3; and,

(c) a nucleotide sequence which specifically hybridizes under stringent conditions, comprising a 0.2x SSC wash at 65°C for 15 minutes, to either strand of a denatured, double-stranded nucleic acid having a nucleotide sequence set forth in SEQ ID NO:2; ~~and~~

wherein expression of the nucleotide sequence~~,~~ in an ~~ascomycetes~~ ascomycete host cell~~,~~ results in the increased production of a polypeptide capable of regulating a gene cluster specifying the production of at least one secondary metabolite selected from the group consisting of a polyketide, a non-ribosomal protein and a hyphal pigment.

9. (Amended) An isolated nucleic acid according to claim 7 wherein the polypeptide encoded by said isolated nucleic acid regulates the activity of a lovastatin biosynthesis gene cluster or a penicillin biosynthesis gene cluster in an ascomycete.

11. (Amended) An expression vector comprising ~~an isolated~~ a nucleic acid according to claim 7 wherein said ~~isolated~~ nucleic acid is ~~in operative association with~~ operatively-linked to one or more regulatory elements.

12. (Amended) A transformed prokaryotic or eukaryotic host cell or cell line comprising ~~an isolated~~ a nucleic acid according to claim ~~7~~ 11.

13. (Amended) A transformed ~~prokaryotic or eukaryotic~~ host cell or cell line according to claim 12 which is an ascomycete host cell or cell line wherein said transformed ~~prokaryotic or eukaryotic~~ ascomycete host cell or cell line is capable of at least a two fold increase in production of a secondary metabolite relative to non-transformed ~~prokaryotic or eukaryotic~~ ascomycete host cell or cell line.

14. (Amended) A method of preparing ~~an isolated~~ a polypeptide ~~comprising LaeA or fragments thereof,~~ capable of regulating secondary metabolite production in an ascomycete comprising ~~the step of~~

(a) culturing a transformed prokaryotic or eukaryotic host cell or cell line of claim 12 under conditions conducive to expression of the polypeptide, and

(b) recovering the expressed polypeptide from the prokaryotic or eukaryotic host cell or cell line in isolated form.

16. (Amended) A method of increasing the amount of a secondary metabolite produced in an ascomycete, comprising ~~the steps of:~~

(a) obtaining an ascomycete capable of producing a secondary metabolite;

(b) transforming said ascomycete with a nucleic acid according to claim ~~7~~ 11; and

(c) culturing said transformed ascomycete under conditions favorable to the expression of the transforming nucleic acid so that an increase in production of the secondary metabolite occurs in the transformed ascomycete as compared to a non-transformed ascomycete.

18. (Amended) A method according to claim 17 wherein the Aspergillus species is ~~A.~~ *Aspergillus nidulans* or ~~A.~~ *Aspergillus terreus*.

20. (Amended) A method according to claim 16 wherein transformation with ~~said~~ a nucleic acid according to claim ~~7~~ 11 ~~overexpresses~~ permits the overexpression of a polypeptide ~~having secondary metabolite gene cluster regulating activity~~ capable of regulating secondary metabolite production in an ascomycete.

23. (Amended) A method of producing an isolated secondary metabolite, comprising ~~steps of:~~

(a) obtaining an ascomycete capable of biosynthesizing a secondary metabolite~~;~~,

(b) transforming said ascomycete with a nucleic acid according to claim ~~7~~ 11,

(c) culturing said transformed ascomycete under conditions conducive to the expression of the transforming nucleic acid thereby increasing production of the secondary metabolite in the transformed ascomycete as compared to a non transformed ascomycete, and

(d) recovering said secondary metabolite from the transformed ascomycete in an isolated form.

25. (Amended) A method according to claim 24 wherein the *Aspergillus* species is ~~*A.*~~ *Aspergillus nidulans* or ~~*A.*~~ *Aspergillus terreus*.

27. (Amended) A method according to claim ~~7~~ 11 ~~overexpresses~~ permits the overexpression of a polypeptide ~~having secondary metabolite gene cluster regulating activity~~ capable of regulating secondary metabolite production in an ascomycete.

33. (Amended) The transformed prokaryotic or eukaryotic host cell or cell line according to claim 12, wherein expression of the polynucleotide results in the increased synthesis of RNA coding for a protein methyltransferase.

34. (Amended) The transformed prokaryotic or eukaryotic host cell or cell line of claim ~~13~~ 12, wherein the host cell or cell line is selected from the group consisting of: ~~fungi~~ fungal cells, ~~bacteria~~ bacterial cells, yeast, insect cells, plant cells and mammalian cells.

36. (Amended) The ~~transformed prokaryotic or eukaryotic host cell or cell line~~ vector according to claim 11, wherein at least one of the regulatory elements is an inducible promoter.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Colin L. Fairman on 27 September 2005.

The following is an examiner's statement of reasons for allowance:

The above examiner's amendment clarifies the intended subject matter by stating the utility disclosed at pages 5-6 of the specification, and taken from the canceled claim 8, in the closing clause of the independent claim 7. Other claim amendments remove unnecessary terms that need not recapitulate the description of claim 7 and ensure that rejoined method of use claims are commensurate in scope with the allowable product of claim 7, where methods of claims 23-27 comprise the production of any secondary metabolite when the transforming DNA of claim 7 is also capable of regulating the production of at least one of the classes of secondary metabolites stated in claim 7.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
27 September 2005

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER